

WHAT IS CLAIMED IS:

1. An isolated polypeptide comprising
  - (a) at least one of (i) the sequence PPPGY (SEQ ID NO:1) and (ii) the sequence LPPAY (SEQ ID NO:2) and
  - (b) at least three domains, each domain comprising the sequence YGXPPXG (SEQ ID NO:3), wherein Y represents a Tyrosine residue, G represents a Glycine residue, L represents a Leucine residue, A represents an Alanine residue, X represents any amino acid residue, and P represents a Proline residue.
2. The isolated polypeptide of claim 1, wherein the polypeptide has a molecular weight of about 32 kDa.
3. The isolated polypeptide of claim 1, wherein the polypeptide comprises 10 domains, each domain comprising the sequence YGXPPXG (SEQ ID NO:3).
4. The isolated polypeptide of claim 1, wherein the polypeptide binds to (a) tyrosine kinase c-Yes and/or (b) an adapter protein, wherein the adapter protein binds to tyrosine kinase c-Yes.
5. The isolated polypeptide of claim 1, wherein the polypeptide induces oocyte activation.
6. The isolated polypeptide of claim 1, wherein the polypeptide comprises the sequence of SEQ ID NO:5, as illustrated in Fig. 1, or conservative variants thereof.

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7. A peptidomimetic of the polypeptide of claim 1.
8. An isolated polynucleotide encoding the polypeptide of claim 1.
9. An isolated polynucleotide encoding the polypeptide of claim 6.
10. The isolated polynucleotide of claim 8, wherein the polynucleotide comprises the sequence of SEQ ID NO:4, as illustrated in Fig. 1, or degenerate variants thereof.
11. A gene comprising the polynucleotide of claim 8.
12. A vector comprising the gene of claim 11.
13. A vector comprising the polynucleotide of claim 8.
14. A host cell comprising the vector of claim 12.
15. A method of producing a polypeptide, the method comprising maintaining the host cell of claim 14 under conditions such that said polypeptide is expressed, then collecting the polypeptide.
16. A fragment of the polypeptide of claim 1, wherein the fragment is antigenic.
17. A fragment of the polypeptide of claim 1, wherein the fragment is biologically active.

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18. A fragment of the polypeptide of claim 1, wherein the fragment binds to tyrosine kinase c-Yes and/or to an adapter protein that binds to tyrosine kinase c-Yes.

19. An antibody that specifically binds to the polypeptide of claim 1.

20. The antibody of claim 19, wherein the antibody is a monoclonal antibody.

21. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the antibody of claim 19.

22. A pharmaceutical composition comprising a pharmaceutically acceptable foam and at least one molecule selected from the group consisting of an antibody that specifically binds to PT32, an antibody that specifically binds to c-Yes, PT32 or a fragment thereof, c-Yes or a fragment thereof, an agonist or antagonist of PT32, and an agonist or antagonist of c-Yes.

23. A method for inducing oocyte activation, the method comprising contacting an oocyte with (a) at least one of (i) the isolated polypeptide of claim 5 or a biologically active fragment thereof and/or (ii) a c-Yes polypeptide or a biologically active fragment thereof, and (b) globozoospermic sperm or round spermatids.

24. A method for inducing oocyte activation, the method comprising contacting an oocyte with a composition consisting essentially of a perinuclear theca protein 32 (PT32), or a biologically active fragment thereof.

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25. A method for enhancing fertility in a mammal, the method comprising expressing in a germ cell of the mammal the polypeptide of claim 5.

26. The method of claim 25, wherein the mammal is a human.

27. The method of claim 25, wherein the mammal is bovine, a pig, a sheep, a goat, a monkey, or a horse.

28. A method for treating globozoospermy, the method comprising expressing in spermatozoa the polypeptide of claim 1.

29. A method for identifying a modulator of oocyte activation, the method comprising  
contacting a test compound with an oocyte,  
treating the oocyte with the polypeptide of claim 5 under conditions sufficient to induce oocyte activation in the absence of the test compound, and  
detecting inhibition or enhancement of oocyte induction as an indication that the test compound is an modulator of oocyte activation.

30. A method for identifying a modulator of oocyte activation, the method comprising

contacting a test compound with (i) the polypeptide of claim 1, or a fragment thereof that binds to c-Yes or to an adapter protein that binds to c-Yes, and (ii) tyrosine kinase c-Yes, or a fragment thereof that binds to PT32 or an adapter protein, under conditions sufficient to permit binding of (i) and (ii) in the absence of the test compound, and

detecting modulation of binding of the polypeptide of claim 1, or the fragment thereof, to the tyrosine kinase c-Yes, or the fragment thereof, as an indication that the test compound is an modulator of oocyte activation.

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31. A method for inhibiting fertilization of a mammalian oocyte, the method comprising inhibiting the interaction of PT32 with tyrosine kinase c-Yes in the oocyte.

32. The method of claim 31, wherein inhibition comprises contacting the oocyte with at least one of (i) an antibody that specifically binds to PT32 and (ii) an antibody that specifically binds to tyrosine kinase c-Yes.

33. A method for inhibiting fertilization, the method comprising introducing into a mammal the polypeptide of claim 1, or an antigenic fragment thereof, such that an immune response is elicited in the mammal.

34. A fusion polypeptide comprising the polypeptide of claim 1, or a fragment thereof, covalently linked to a second polypeptide.

35. A vaccine comprising the fusion polypeptide of claim 34 and an adjuvant.

36. A vaccine comprising the polypeptide of claim 16 and an adjuvant.

37. A method for diagnosing diminished fertility in a mammal, the method comprising measuring the level of the polypeptide of claim 1 in spermatozoa of the mammal, wherein diminished levels of the polypeptide of claim 1 indicate that the mammal suffers from diminished fertility.

38. A method for diagnosing diminished fertility in a mammal, the method comprising measuring the level of tyrosine kinase c-Yes in a germ cell of the mammal, wherein diminished levels of tyrosine kinase c-Yes indicate that the mammal suffers from diminished fertility.

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39. A method for diagnosing abnormal spermiogenesis in a mammal, the method comprising comparing (i) the pattern of distribution of the polypeptide of claim 1 throughout mature spermatozoa of the mammal with (ii) the pattern of distribution of the polypeptide of claim 1 throughout healthy, mature spermatozoa, wherein an abnormal distribution pattern is an indication that spermiogenesis in the mammal is abnormal.

40. A method for diagnosing abnormal spermiogenesis in a mammal, the method comprising comparing (i) the pattern of the distribution of tyrosine kinase c-Yes throughout mature spermatozoa of the mammal with (ii) the pattern of the distribution of tyrosine kinase c-Yes throughout healthy, mature spermatozoa, wherein an abnormal distribution pattern is an indication that spermiogenesis in the mammal is abnormal.

41. A method for determining whether spermiogenesis is abnormal in a mammal, the method comprising determining the pattern of the distribution of PT32 throughout spermatozoa of the mammal, wherein the failure of the PT32 to be localized either (i) between the acrosome and the nucleus of the spermatozoa or (ii) on a post-acrosomal portion of the head of the spermatozoa is an indication that spermiogenesis is abnormal in the mammal.

42. A transgenic non-human mammal whose germ cells contain a disruption in the endogenous gene encoding PT32, wherein said disruption comprises the insertion of a selectable marker sequence, and wherein said disruption results in the lack of expression or function of said PT32.

43. The transgenic mammal of claim 42, wherein the mammal is a mouse, bovine, or a monkey.

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44. A method for enhancing oocyte activation, the method comprising contacting a mammalian oocyte with tyrosine kinase c-Yes, or a biologically active fragment thereof.

45. A transgenic non-human mammal whose germ cells contain a disruption in the endogenous gene encoding tyrosine kinase c-Yes, wherein said disruption comprises the insertion of a selectable marker sequence, and wherein said disruption results in the lack of expression or function of said tyrosine kinase c-Yes.

46. The isolated polypeptide of claim 1, wherein the polypeptide has a molecular weight of about 30 kDa.

47. The isolated polypeptide of claim 1, wherein the polypeptide comprises the sequence of SEQ ID NO:12, as illustrated in Fig. 4B, or conservative variants thereof.

48. An isolated polynucleotide encoding the polypeptide of claim 47.

49. The isolated polypeptide of claim 1, wherein the polypeptide binds to phospholipase C.

50. The isolated polypeptide of claim 1, wherein the polypeptide is a component of a phospholipase C signal transduction pathway.

51. A method for enhancing the ability of round spermatids to activate oocytes, the method comprising expressing in round spermatids the polypeptide of claim 1.

52. An isolated polypeptide comprising

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- (a) the sequence PPXY (SEQ ID NO:8) and
- (b) at least three domains, each domain comprising the sequence YGXPPXG (SEQ ID NO:3), wherein Y represents a Tyrosine residue, G represents a Glycine residue, X represents any amino acid residue, and P represents a Proline residue.

53. An isolated polynucleotide encoding the polypeptide of claim 52.

54. A WW domain binding protein comprising amino acid residues 61 to 97 of SEQ ID NO:12, or conservative variants thereof.

55. An isolated polypeptide comprising amino acid residues 61 to 97 of SEQ ID NO:12.

56. A method for inducing oocyte activation, the method comprising contacting an oocyte with (i) an isolated polypeptide comprising the sequence of SEQ ID NO:18 or (ii) a biologically active fragment thereof, or conservative variants of (i) or (ii).

57. A method for enhancing fertility in a mammal, the method comprising expressing in a germ cell of the mammal an isolated polypeptide comprising (i) the sequence of SEQ ID NO:18 or (ii) a biologically active fragment thereof, or conservative variants of (i) or (ii).

58. A method for identifying a modulator of oocyte activation, the method comprising

contacting a test compound with an oocyte;

treating the oocyte with the an isolated polypeptide comprising (i) the sequence of SEQ ID NO:18 or (ii) a biologically active fragment thereof, or

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conservative variants of (i) or (ii), under conditions sufficient to induce oocyte activation in the absence of the test compound; and

detecting inhibition or enhancement of oocyte induction as an indication that the test compound is a modulator of oocyte activation.

59. The isolated polypeptide of claim 1, wherein the polypeptide is a human or bovine polypeptide.

60. The isolated polynucleotide of claim 8, wherein the polynucleotide is a human or bovine polynucleotide.

61. An isolated polynucleotide comprising a sequence that is at least 75% identical to nucleotides 36 to 933 of SEQ ID NO: 4.

62. An isolated polynucleotide comprising a sequence that is at least 75% identical to nucleotides 1 to 705 of SEQ ID NO: 11.

63. An isolated polypeptide comprising a sequence that is at least 75% identical to SEQ ID NO:5.

64. An isolated polypeptide comprising a sequence that is at least 75% identical to SEQ ID NO:12.

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